

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

Claims 1-13 (cancelled)

Claim 14 (previously presented): A cholesterol-lowering therapy method, which method comprises the administration of melagatran or a pharmaceutically acceptable derivative thereof to a patient in need of such therapy.

Claim 15 (cancelled)

Claim 16 (previously presented): The method of Claim 14 wherein the therapy/treatment results in a decrease in serum levels of cholesterol, low-density lipoproteins, very low-density lipoproteins, triglycerides and/or apolipoprotein B; and/or an increase in serum levels of high-density lipoproteins and/or apolipoprotein A-I.

Claim 17 (cancelled)

Claim 18 (previously presented): The method of Claim 14, wherein the method comprises administering a prodrug of melagatran.

Claim 19 (previously presented): The method of Claim 18, wherein the method comprises delivering a prodrug of the formula:

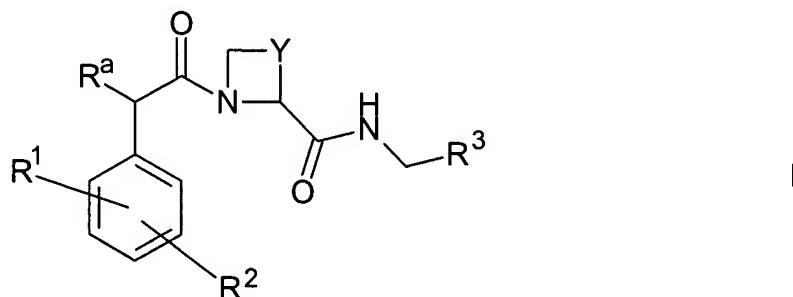


wherein  $R^1$  represents linear or branched  $C_{1-6}$  alkyl and the OH group replaces one of the amidino hydrogens in Pab.

Claim 20 (previously presented): The method of Claim 19, wherein  $R^1$  represents methyl, ethyl or propyl.

Claim 21 (previously presented): The method of Claim 20, wherein R<sup>1</sup> represents ethyl.

**Claim 22 (withdrawn):** A cholesterol-lowering therapy method, which method comprises the administration of a thrombin inhibitor of formula I,



wherein

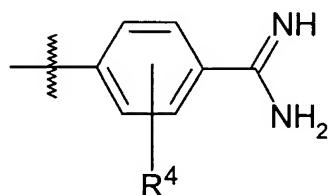
R<sup>a</sup> represents -OH or -CH<sub>2</sub>OH;

R<sup>1</sup> represents at least one optional halo substituent;

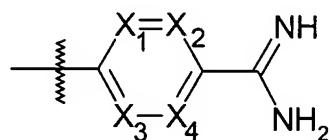
$R^2$  represents one or two  $C_{1-3}$  alkoxy substituents, the alkyl parts of which substituents are themselves substituted with one or more fluoro substituents:

Y represents  $-\text{CH}_2-$  or  $-(\text{CH}_2)_2-$ ; and

$R^3$  represents a structural fragment of formula I(i) or I(ii):



I(i)



I(ii)

wherein

$R^4$  represents H or one or more fluoro substituents; and

one or two of  $X_1$ ,  $X_2$ ,  $X_3$ , and  $X_4$  represent -N- and the others represent -CH-, or a pharmaceutically acceptable derivative thereof.

to a patient in need of such therapy.

**Claim 23 (withdrawn):** The method of Claim 22, wherein the thrombin inhibitor or derivative is:

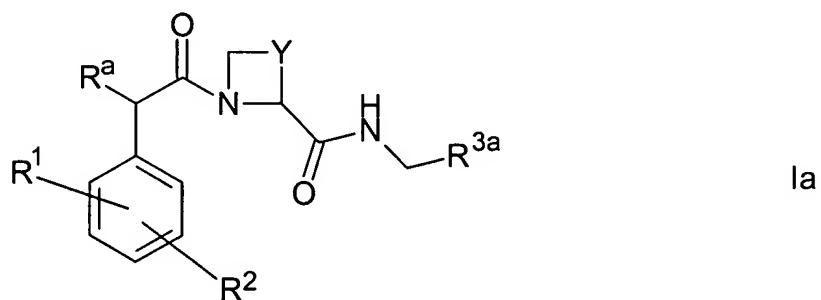
Ph(3-Cl)(5-OCHF<sub>2</sub>)-(R)CH(OH)C(O)-(S)Aze-Pab;

Ph(3-Cl)(5-OCHF<sub>2</sub>)-(R)CH(OH)C(O)-(S)Aze-Pab(2,6-diF); or

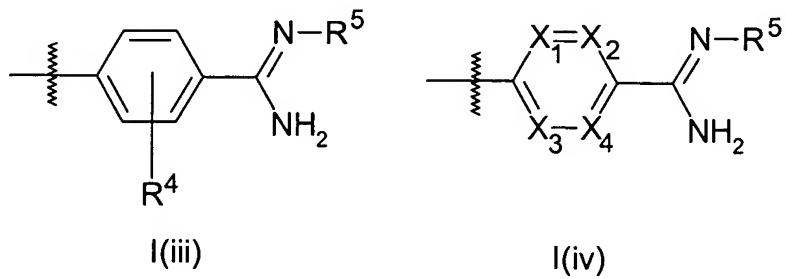
Ph(3-Cl)(5-OCH<sub>2</sub>CH<sub>2</sub>F)-(R)CH(OH)C(O)-(S)Aze-Pab.

**Claim 24 (withdrawn):** The method of Claim 22, wherein the thrombin inhibitor or derivative is a prodrug of a thrombin inhibitor.

Claim 25 (withdrawn): The method of Claim 24, wherein the prodrug is of formula Ia,



wherein  $R^{3a}$  represents a structural fragment of formula I(iii) or I(iv):



wherein R<sup>5</sup> represents OR<sup>6</sup> or C(O)OR<sup>7</sup>;

$R^6$  represents H,  $C_{1-10}$  alkyl,  $C_{1-3}$  alkylaryl, or  $C_{1-3}$  alkyloxyaryl, the alkyl parts of which latter two groups are optionally interrupted by one or more oxygen atoms, and the aryl parts of

which latter two groups are optionally substituted by one or more substituents selected from halo, phenyl, methyl or methoxy, which latter three groups are also optionally substituted by one or more halo substituents; and

$R^7$  represents  $C_{1-10}$  alkyl, optionally interrupted by one or more oxygen atoms;  $C_{1-3}$  alkylaryl; or  $C_{1-3}$  alkyloxyaryl, the alkyl parts of which latter two groups are optionally interrupted by one or more oxygen atoms, and the aryl parts of which latter two groups are optionally substituted by one or more substituents selected from halo, phenyl, methyl or methoxy, which latter three groups are also optionally substituted by one or more halo substituents.

Claim 26 (withdrawn): The method of Claim 25, wherein the prodrug is:

$Ph(3-Cl)(5-OCHF_2)-(R)CH(OH)C(O)-(S)Aze-Pab(OMe)$ ;  
 $Ph(3-Cl)(5-OCHF_2)-(R)CH(OH)C(O)-(S)Aze-Pab(2,6-diF)(OMe)$ ; or  
 $Ph(3-Cl)(5-OCH_2CH_2F)-(R)CH(OH)C(O)-(S)Aze-Pab(OMe)$ .

Claim 27 (withdrawn): A combination product comprising:

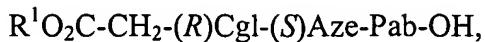
- (A) a low molecular weight thrombin inhibitor, or a pharmaceutically-acceptable derivative thereof; and
- (B) another cholesterol-lowering, or lipid-lowering/modifying, therapeutic agent, wherein each of components (A) and (B) is formulated in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

Claims 28-29 (cancelled)

Claim 30 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is melagatran.

Claim 31 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is a prodrug of melagatran.

Claim 32 (withdrawn): The combination product of Claim 31, wherein the prodrug is of the formula:

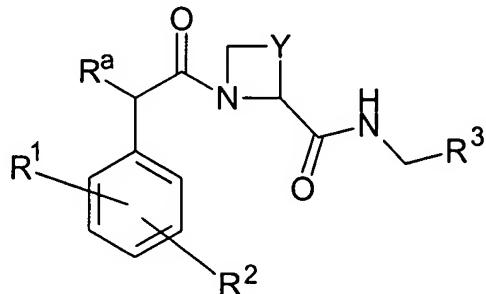


wherein  $R^1$  represents linear or branched  $C_{1-6}$  alkyl and the OH group replaces one of the amidino hydrogens in Pab.

Claim 33 (withdrawn): The combination product of Claim 32, wherein  $R^1$  represents methyl, ethyl, or propyl.

Claim 34 (withdrawn): The combination product of Claim 33, wherein  $R^1$  represents ethyl.

Claim 35 (currently amended): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is a compound of formula I,



I

wherein

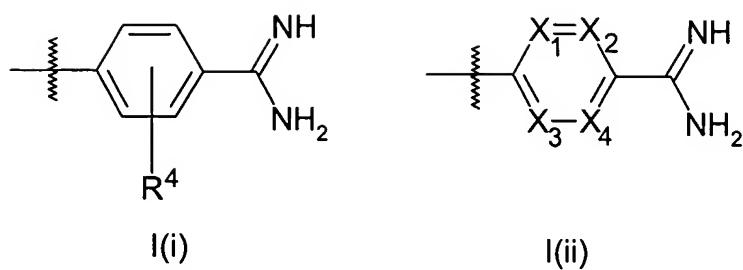
$R^a$  represents -OH or -CH<sub>2</sub>OH;

$R^1$  represents at least one optional halo substituent;

$R^2$  represents one or two  $C_{1-3}$  alkoxy substituents, the alkyl parts of which substituents are themselves substituted with one or more fluoro substituents;

$Y$  represents -CH<sub>2</sub>- or -(CH<sub>2</sub>)<sub>2</sub>-; and

$R^3$  represents a structural fragment of formula I(i) or I(ii):



wherein

R<sup>4</sup> represents H or one or more fluoro substituents; and

one or two of X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, and X<sub>4</sub> represent -N- and the others represent -CH-.

Claim 36 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:

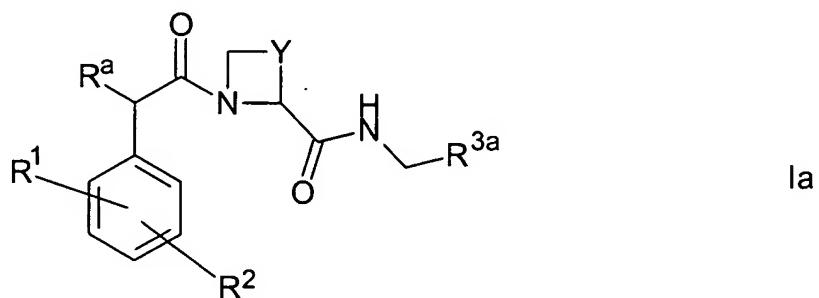
Ph(3-Cl)(5-OCHF<sub>2</sub>)-(R)CH(OH)C(O)-(S)Aze-Pab;

Ph(3-Cl)(5-OCHF<sub>2</sub>)-(R)CH(OH)C(O)-(S)Aze-Pab(2,6-diF); or

Ph(3-Cl)(5-OCH<sub>2</sub>CH<sub>2</sub>F)-(R)CH(OH)C(O)-(S)Aze-Pab.

Claim 37 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is a prodrug of a thrombin inhibitor.

Claim 38 (currently amended): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is a prodrug is of formula Ia,



wherein

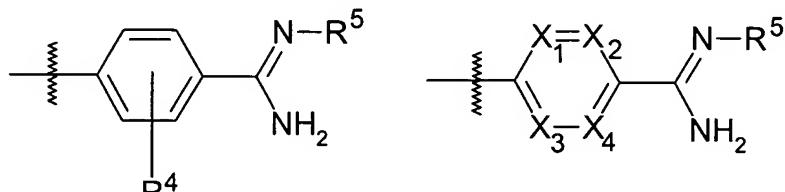
R<sup>a</sup> represents -OH or -CH<sub>2</sub>OH;

R<sup>1</sup> represents at least one halo substituent;

R<sup>2</sup> represents one or two C<sub>1-3</sub> alkoxy substituents, the alkyl parts of which substituents are themselves substituted with one or more fluoro substituents;

Y represents -CH<sub>2</sub>- or -(CH<sub>2</sub>)<sub>2</sub>-;

R<sup>3a</sup> represents a structural fragment of formula I(iii) or I(iv):



I(iii)

I(iv)

wherein

R<sup>4</sup> represents H or one or more fluoro substituents;

one or two of X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, and X<sub>4</sub> represent -N- and the others represent -CH-;

R<sup>5</sup> represents OR<sup>6</sup> or C(O)OR<sup>7</sup>;

R<sup>6</sup> represents H, C<sub>1-10</sub> alkyl, C<sub>1-3</sub> alkylaryl or C<sub>1-3</sub> alkyloxyaryl, the alkyl parts of which latter two groups are optionally interrupted by one or more oxygen atoms, and the aryl parts of which latter two groups are optionally substituted by one or more substituents selected from halo, phenyl, methyl or methoxy, which latter three groups are also optionally substituted by one or more halo substituents; and

R<sup>7</sup> represents C<sub>1-10</sub> alkyl, which latter group is optionally interrupted by one or more oxygen atoms; C<sub>1-3</sub> alkylaryl; or C<sub>1-3</sub> alkyloxyaryl, the alkyl parts of which latter two groups are optionally interrupted by one or more oxygen atoms, and the aryl parts of which latter two groups are optionally substituted by one or more substituents selected from halo, phenyl, methyl or methoxy, which latter three groups are also optionally substituted by one or more halo substituents.

Claim 39 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:

Ph(3-Cl)(5-OCHF<sub>2</sub>)-(R)CH(OH)C(O)-(S)Aze-Pab(OMe);

Ph(3-Cl)(5-OCHF<sub>2</sub>)-(R)CH(OH)C(O)-(S)Aze-Pab(2,6-diF)(OMe); or

Ph(3-Cl)(5-OCH<sub>2</sub>CH<sub>2</sub>F)-(R)CH(OH)C(O)-(S)Aze-Pab(OMe).

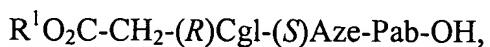
Claim 40 (withdrawn): The combination product of Claim 27, wherein the other therapeutic agent is a statin.

Claim 41 (withdrawn): The combination product of Claim 27, wherein the other therapeutic agent is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.

Claims 42-44 (cancelled)

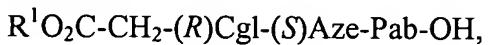
Claim 45 (withdrawn): The method of Claim 22, wherein the therapy/treatment results in a decrease in serum levels of cholesterol, low-density lipoproteins, very low-density lipoproteins, triglycerides and/or apolipoprotein B; and/or an increase in serum levels of high-density lipoproteins and/or apolipoprotein A-I.

Claim 46 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is of the formula:



wherein R<sup>1</sup> represents linear or branched C<sub>1-6</sub> alkyl and the OH group replaces one of the amidino hydrogens in Pab, and the other therapeutic agent is a statin.

Claim 47 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is of the formula:



wherein R<sup>1</sup> represents linear or branched C<sub>1-6</sub> alkyl and the OH group replaces one of the amidino hydrogens in Pab, and the other therapeutic agent is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.

Claim 48 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is of the formula:



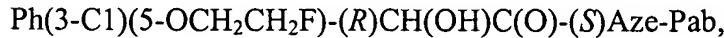
wherein Et represents ethyl and the OH group replaces one of the amidino hydrogens in Pab, and the other therapeutic agent is a statin.

Claim 49 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is of the formula:



wherein Et represents ethyl and the OH group replaces one of the amidino hydrogens in Pab, and the other therapeutic agent is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.

Claim 50 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:



and the other therapeutic agent is a statin.

Claim 51 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:



and the other therapeutic agent is a statin.

Claim 52 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:



Ph(3-Cl)(5-OCHF<sub>2</sub>)-(R)CH(OH)C(O)-(S)Aze-Pab (2,6-diF); or

Ph(3-C1)(5-OCH<sub>2</sub>CH<sub>2</sub>F)-(R)CH(OH)C(O)-(S)Aze-Pab,

and the other therapeutic agent is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.

Claim 53 (withdrawn): The combination product of Claim 27, wherein the thrombin inhibitor or derivative is:

Ph(3-Cl)(5-OCHF<sub>2</sub>)-(R)CH(OH)C(O)-(S)Aze-Pab(OMe);

Ph(3-Cl)(5-OCHF<sub>2</sub>)-(R)CH(OH)C(O)-(S)Aze-Pab(2,6-diF)(OMe); or

Ph(3-C1)(5-OCH<sub>2</sub>CH<sub>2</sub>F)-(R)CH(OH)C(O)-(S)Aze-Pab(OMe),

and the other therapeutic agent is lovastatin, pravastatin, fluvastatin, simvastatin, atorvastatin, pitavastatin, or rosuvastatin.